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(54) Title: TRANSGENIC MAMMALS HAVING HUMAN Ig LOCI INCLUDING PLURAL V_H AND V_K REGIONS AND ANTIBODIES PRODUCED THEREFROM

(57) Abstract

The present invention relates to transgenic non-human animals that are engineered to contain human immunoglobulin gene loci. In particular, animals in accordance with the invention possess human Ig loci that include plural variable (V_H and V_K) gene regions. Advantageously, the inclusion of plural variable region genes enhances the specificity and diversity of human antibodies produced by the animal. Further, the inclusion of such regions enhances and reconstitutes B-cell development to the animals, such that the animals possess abundant mature B-cells secreting extremely high affinity antibodies.

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INTERNATIONAL SEARCH REPORT

Internal Application No
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A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 A01K67/027 C07K16/00 C07K16/24 C07K16/28 //C12N15/85,
 C12N15/90

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 6 A01K C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>A. JAKOBOWITS ET AL., : "Production of antigen-specific human antibodies from mice engineered with human heavy and light chain YACs" <i>ANNALS OF THE NEW YORK ACADEMY OF SCIENCES</i>, <i>vol. 764, 1995, NEW YORK, NY, US,</i> <i>pages 525-535, XP002067728</i> <i>see the whole document but specially pages 533-534</i></p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/-</p>	1-16

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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International Application No

PCT/US 97/23091

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94 25585 A (GENPHARM INT) 10 November 1994 cited in the application see page 1, line 19-33 see page 6, line 24 - page 7, line 23 see page 11, line 6 - page 12, line 19 see page 23, line 25 - page 24, line 7 see page 48, line 35 - page 49, line 22; examples 1-5 see page 185, line 26 - page 190, line 31 see page 198, line 18-30 see page 202, line 16-36	1,2, 6-10,16, 24
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A	M. BRUGGEMAN AND N.S. NEUBERGER: "Strategies for expressing human antibody repertoires in transgenic mice" IMMUNOLOGY TODAY, vol. 17, no. 8, 1 August 1996, OXFORD, GB, pages 391-397, XP002067729 cited in the application see the whole document	1-28
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	A. JAKOBOVITS ET AL., : "Human immunity in mice engineered with megabase human heavy and kappa light chain YACs" THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, vol. 99, no. 1, part 2, 1 January 1997, SAINT LOUIS, MO, US, page S113 XP002067604 see abstract ---	1-15
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Information on patent family members

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